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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification 5 :</b>  A61K 7/48, 31/71		<b>A1</b>	<b>(11) International Publication Number:</b> WO 93/20796  <b>(43) International Publication Date:</b> 28 October 1993 (28.10.93)
<b>(21) International Application Number:</b> PCT/US93/03325			<b>(81) Designated States:</b> AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
<b>(22) International Filing Date:</b> 7 April 1993 (07.04.93)			
<b>(30) Priority data:</b> 07/865,562 9 April 1992 (09.04.92) US			
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**(54) Title:** METHOD AND COMPOSITION FOR TREATING ACNE

**(57) Abstract**

The present invention provides topical compositions of a peroxide of an organic acid, e.g., benzoyl peroxide and clindamycin and its derivatives, such as clindamycin phosphate, which are useful for treating acne vulgaris. Such compositions may further include a surfactant including a sulfonic radical.

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## METHOD AND COMPOSITION FOR TREATING ACNE

### FIELD OF THE INVENTION

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This invention relates to a method and composition for treating acne vulgaris.

### BACKGROUND OF THE ART

10

Acne vulgaris is an inflammatory disease of the sebaceous glands characterized by an eruption of the skin, often pustular in nature but not suppurative. Acne is a common affliction of the adolescent and affects a small but significant percentage of the adult 15 population. Acne involvement results in unsightly lesions, particularly on the face, and in some cases results in severe scarring.

Various topical agents are utilized in the treatment of acne and these include sulfur, resorcinol, salicylic acid, benzoyl peroxide, 20 retinoids and topical antibiotics. An effective anti-acne agent (or composition) must exhibit the following activities:

- (a) a sebostatic activity so as to inhibit hyperseborrhea;
- (b) a keratolytic and comedolytic activity so as to avoid hyperkeratosis of the follicles and to permit removal of comedos;
- (c) a bacteriostatic activity so as to inhibit the activity of *Propionibacterium acnes*.

30 Nevertheless, acne vulgaris is seldom cured and only can be contained with difficulty.

The antibiotic clindamycin has been used, topically, to treat acne vulgaris. (See U.S. Patent 3,969,516, to Stoughton.) Various 35 references discuss the use of vehicle formulations to enhance the efficacy of topically-applied clindamycin. (See U.S. Patents 3,932,653; 3,989,816; 3,991,203; 4,132,781; 4,671,956; 4,746,675; 4,789,667; 4,803,228

and 4,882,359.) Clindamycin salts, clindamycin derivatives, and various dosage forms of clindamycin have also been discussed as a treatment for acne vulgaris. (See U.S. Patent 3,849,396; 4,621,075 and 4,916,118.) Finally, combinations of clindamycin and other 5 compounds active for the treatment of acne vulgaris are disclosed in U.S. Patents, 4,323,558; 4,505,896; 4,607,101; 4,906,617; 4,942,031 and 4,018,918.

10 Benzoyl peroxide has been suggested for treating acne vulgaris. (See U.S. Patent 4,387,107.) For many years, benzoyl peroxide has been proven to be a particularly powerful keratolytic and anti-seborrhic agent, as well as being endowed with antibacterial properties. Topical benzoyl peroxide compositions, including a vehicle to enhance the efficacy thereof, are known (See 15 U.S. Patent 4, 411,893). Topical compositions of benzoyl peroxide combination with antibiotics are also known. (See U.S. Patents 4,407,794; 4,692,329 and 4,387,107)

20 Peroxides, other than benzoyl peroxide, have been suggested for treatment of acne vulgaris, alone, or in combination with other compounds useful in treating acne vulgaris. (See U.S. Patents 4,607,101 and 4,906,617.) These peroxides are suggested as having certain advantages, e.g. stability over benzoyl peroxide. U.S. Patent 4,671,956 identifies the problem of benzoyl peroxide decomposing 25 coingredients in topical formulations to thereby cause itching upon application. It is suggested that this problem may be solved by including a sunscreen in the topical formulation to retard this decomposition effect of benzoyl peroxide.

30 In view of the above, it is apparent that there is a great deal of interest in formulating topical compositions for the treatment of acne vulgaris, such compositions utilizing as an active ingredient clindamycin or benzoyl peroxide, alone, or in combination with other active ingredients for the treatment of acne vulgaris. 35 Furthermore, it is apparent that there are stability problems associated with topical compositions including benzoyl peroxide,

alone, or in combination with other pharmacologically-active compounds.

5       Therefore, one object of the instant invention is to provide a method of treating acne vulgaris with a topical composition including benzoyl peroxide and clindamycin.

10      It is another object of the invention to provide compositions of benzoyl peroxide and clindamycin effective for use in the topical treatment of acne vulgaris.

15      It is another object of this invention to provide stable compositions for the topical treatment of acne vulgaris.

20      Another object of the invention is to provide topical compositions of benzoyl peroxide and clindamycin that are stable to storage over extended periods of time at ambient conditions.

25      Other objects and advantages of the instant invention will become apparent from a careful reading of the specification below.

#### SUMMARY OF THE INVENTION

30      The present invention provides a method for treating acne vulgaris by topically applying a composition of benzoyl peroxide and clindamycin in a therapeutically-effective amount. The antibiotic clindamycin (free base), or its pharmaceutically acceptable salts or prodrugs (e.g., clindamycin phosphate, clindamycin hydrochloride), may be applied in an amount sufficient to provide from about 0.1 to about 10 percent, and preferably from about 0.5 to about 5 percent by weight, clindamycin. Benzoyl peroxide, which has keratolytic and antiseborrheic properties, may be present in an amount sufficient to provide from about 0.1 to about 30 percent, and preferably from about 2.5 to about 10 percent, by weight, benzoyl peroxide. The benzoyl peroxide may more preferably be used as hydrous benzoyl peroxide and may be suspended preferably in the

form of microparticles. The above described topical composition may be in the form of a solution, gel, ointment, cream, a liquid suspension or emulsion or a stick base. The topical composition of this invention may further include a surfactant preferably comprising at least one sulfonic radical, e.g., long-chain alkyl sulfonates or alkyl aryl sulfonates. The surfactant may comprise from about 0.01 to about 5 percent, by weight, and preferably from 0.025 to about 1 percent, of the above topical composition. Surfactants which are useful in the method and composition of this invention include dioctyl sodium sulfosuccinate and sodium dodecylbenzenesulfonate.

#### DETAILED DESCRIPTION OF THE INVENTION

15 The compositions of this invention are administered topically to treat acne vulgaris. That is, the compositions may be applied as a solution, gel, ointment, cream, a liquid suspension or emulsion or a stick base. Thus, it is preferred that such compositions include a pharmaceutically acceptable carrier that enhances the efficacy of such topical administration. Pharmaceutically acceptable carriers include conventional emulsifiers, such as fatty alcohols, glycol ethers and esters of fatty acids; conventional emollients, such as isopropyl and butyl esters of fatty acids, e.g. isopropyl myristate; humectants such as glycerin, propylene glycol, polyethylene glycol; and alcohols and acetone; oils such as mineral oil, petroleum oil, oil extracts from animal or vegetable sources; conventional stabilizers including antioxidants and preservatives. The formulation may also include agents, such as urea, to improve the hydration of the skin. In addition to the foregoing conventional formulations, the topical compositions may include penetration-enhancing agents such as 1-pyrrolidone and N-lower alkyl-2-pyrrolidones, such as N-methyl-2-pyrrolidone; and 1-substituted azacycloalkan-2-ones such as, for example, 1-n-dodecylazacycloheptan-2-one and other compounds disclosed in U.S. Pat. No. 3,989,816. Longer chain sulfoxides, e.g., n-octyl methyl sulfoxide and hexamethylene-lauramide and the other penetration-

enhancing agents disclosed in U.S. Patent No. 4,743,588, may also be included in the formulations of this invention. The amount of these compounds which may be used in the present invention ranges from about 0.1 to 25 percent and preferably about 1 to 15 percent by weight of the composition.

12

The amount of the composition to be administered will obviously be an effective amount for the desired result expected therefrom. This, of course, will be ascertained by the ordinary skill of the practitioner. In accordance with the usual prudent formulating practices, a dosage near the lower end of the useful range of the particular agent may be employed initially and the dosage increased as indicated from the observed response, as in the routine procedure of the physician.

10

15

In carrying out the novel method employing the topical route, the active ingredient(s) formulated, for example, as a gel or lotion or suspension, is applied to the affected area of the skin at a rate varying from 0.2 mg per square cm of skin surface per day up to 10 mg per square cm of skin surface per day until the appearance of the affected skin has returned to normal. The gel or lotion or suspension is generally applied for several days.

20

25

The topical compositions of this invention may be applied to the face of a patient with acne 2 to 4 times daily with the result that open and closed comedones are markedly reduced within two weeks.

30

The invention is further illustrated by the following formulations and examples which are illustrative of a specific mode of practicing the invention and is not intended as limiting the scope of the claims.

35

The following gel formulations are prepared by dispersing a polyacrylic acid, e.g. Carbomer 940, available from B.F. Goodrich, into water. To this dispersion is added a dispersion of hydrous

benzoyl peroxide in a solution of clindamycin phosphate, edetate disodium and a surfactant comprising a sulfonate radical. The pH of the resulting dispersion may be buffered with NaOH and a mixture of citric acid monohydrate, and sodium citrate dihydrate.

5

### Formulation 1

Gel containing dioctyl sodium sulfosuccinate and citrate buffer

		Percent
10	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide <sup>1</sup>	7.332
	Carbomer 940 <sup>2</sup>	0.900
	Docusate sodium	0.150
	Disodiumedetate	0.050
15	Citric acid monohydrate	0.096
	Sodium citrate dihydrate	0.264
	Sodium hydroxide	0.140
	Purified water	89.860

20

### Formulation 2

Gel containing sodium dodecylbenzenesulfonate and citrate buffer.

		Percent
25	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Carbomer 940	0.900
	Sodium dodecylbenzenesulfonate	0.170
	Disodiumedetate	0.050
	Sodium citrate dihydrate	0.264
30	Citric acid monohydrate	0.096
	Sodium hydroxide	0.140
	Purified water	89.860

<sup>1</sup>Hydrous benzoyl peroxide includes about 70% by weight benzoyl peroxide as an active ingredient.

<sup>2</sup>Carbopol or carbomer resins are synthetic, high molecular acrylic acid cross-linked to different extents with a polyalkenyl ether (alkyl ethers of either sucrose or pentaerythritol).

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Formulation 3

Gel containing sodium dodecylbenzene sulfonate and citrate buffer

		Percent
5	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Carbomer 940	0.900
	Sodium dodecylbenzenesulfonate	0.420
10	Disodiumedetate	0.050
	Sodium citrate dihydrate	0.264
	Citric acid monohydrate	0.096
	Sodium hydroxide	0.140
	Purified water	89.610

15

Formulation 4

Gel in propylene glycol and water containing dioctyl sodium sulfosuccinate and citrate buffer

		Percent
20	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Carbomer 940	0.900
	Docusate sodium	0.150
25	Disodiumedetate	0.050
	Sodium citrate dihydrate	0.200
	Citric acid monohydrate	0.134
	Sodium hydroxide	0.100
	Propylene glycol	30.000
30	Purified water	59.946

EXAMPLE 1

35 Formulations of Examples 1 and 2 were tested for stability to storage in sealed ointment jars at 5° C. and 23° C. The results are reported in Table I below.

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TABLE I

## Formulation 1

## PERCENT CLINDAMYCIN REMAINING

		5° C.	23° C.
5	1 month	100.2	95.1
	2 months	100.3	94.2
	3 months	101.1	93.0
10	6 months	102.5	

## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C.
15	1 month	95.7	96.4
	2 months	96.9	97.9
	3 months	105.5	103.7
	6 months	101.1	99.0

## Formulation 2

## PERCENT CLINDAMYCIN REMAINING

		5° C.	23° C.
20	1 month	99.1	94.4
	2 months	99.9	92.5
	3 months	101.3	89.6
25	6 months	100.3	

## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C.
30	1 month	97.6	96.1
	2 months	98.2	97.3
	3 months	101.8	101.9
	6 months	97.6	97.9

As can be determined from the above data, the topical compositions of the invention, including both clindamycin and benzoyl peroxide, surprisingly, are stable to storage. It is believed that this stability is a result of the stabilization of the topical compositions by the sulfonate radical-containing surfactant.

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EXAMPLE 2

Formulations 3 and 4 were also tested for stability to storage as in Example 1 above. The results are reported in Table 2 below.

5

TABLE 2

## Formulation 3

## PERCENT CLINDAMYCIN REMAINING

		5° C.	23° C
10	1 month	99.2	90.9
	2 months	99.3	85.8
	3 months	101.2	
	6 months	102.0	

15

## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C
15	1 month	98.2	96.1
	2 months	99.1	97.4
	3 months	103.8	
20	6 months	104.1	

## Formulation 4

## PERCENT CLINDAMYCIN REMAINING

		5° C	23° C
25	1 month	98.7	93.7
	2 months	99.2	89.2
	3 months	100.3	
	6 months	96.7	

30

## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C
30	1 month	97.3	96.4
	2 months	97.2	95.1
	3 months	100.3	
35	6 months	96.4	

These topical compositions of the invention also showed excellent stability to storage.

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Formulation 5

Gel containing docusate sodium

The following gel formulation was prepared as described above  
5 except that no buffer was utilized:

		Percent
	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Carbomer 940	0.900
10	Docusate sodium	0.150
	Disodiumedetate	0.050
	Sodium hydroxide	0.180
	Purified water	90.20

15

EXAMPLE 3

Formulation 5 was tested for storage stability. The results are reported in Table 3, below

20

TABLE 3

## Formulation 5

## PERCENT CLINDAMYCIN REMAINING

		5° C.	23° C.
25	1 month	98.7	98.3
	2 months	95.9	96.7
	3 months	100.6	90.7
	6 months	101.2	

30

## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C.
35	1 month	97.5	97.5
	2 months	96.3	95.0
	3 months	95.7	95.2

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Formulation 6

5 A cream formulation without dioctyl sodium sulfosuccinate was prepared in the form of an oil-in-water emulsion. This cream formulation had the following composition:

		Percent
	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
10	Cetostearyl alcohol	4.000
	Cetearyl octanoate	4.000
	Glyceryl stearate and PEG-100 stearate <sup>3</sup>	2.000
	Carbomer 934P <sup>4</sup>	0.500
	Trolamine	0.500
15	Brij® 30 (laureth-4) <sup>5</sup>	0.250
	Disodium edetate	0.050
	Purified water	80.180

EXAMPLE 4

20 Formulation 6 was tested for storage stability. The results are reported in Table 4 below.

25 TABLE 4  
Formulation 6

		PERCENT CLINDAMYCIN REMAINING	5° C.	23° C
	1 month		102.70	101.00
	2 months		101.00	96.50
30	3 months		100.50	89.20
	6 months		101.30	

<sup>3</sup>Glyceryl stearate and polyoxyethylene (100) stearate in combination is an acid-stable, self-emulsifying system available commercially as Arlacel®165 (ICI Americas).

<sup>4</sup>Carbomer 934P is a high molecular weight polymer of acrylic acid cross-linked with a polyalkenyl polyether.

<sup>5</sup>Brij® 30 is a polyoxyethylene (4) lauryl ether and functions as an emulsifier.

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## PERCENT BENZOYL PEROXIDE REMAINING

		5° C.	23° C
5	1 month	97.6	98.1
	2 months	97.6	95.9
	3 months	95.3	96.0
	6 months	97.8	

Further formulation work was done to obtain stable compositions containing 1.188 percent clindamycin phosphate (equivalent to 1 percent clindamycin) and 7.332 percent hydrous benzoyl peroxide (equivalent to 5 percent benzoyl peroxide, anhydrous) and 3-month stability data were collected for both the active ingredients in these formulations. The detailed compositions of the formulations and the results of stability evaluations are as follows:

Formulation 7

20 Carbomer gel containing 0.45% sodium metabisulfite and 0.05% docusate sodium

	Percent
	1.188
	7.332
	0.450
25.	0.050
	0.050
	0.500
	0.900
30.	0.140
	89.890

Formulation 8

35 Carbomer gel containing 0.1% sodium metabisulfite, 0.1% propyl gallate and 0.1% docusate sodium in citrate buffer (citric acid and sodium citrate).

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		Percent
5	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Sodium metabisulfite	0.100
	Propyl gallate, 20% solution	0.500
	Disodiumedetate	0.100
	Citric acid monohydrate	0.096
10	Sodium citrate dihydrate	0.264
	Carbomer 940	0.900
	Docusate sodium	0.014
	Sodium hydroxide	0.140
	Purified water	89.280

Formulation 9

15 Carbomer gel containing 0.1% sodium metabisulfite, 0.1% propyl gallate, 0.025% docusate sodium and 5% glycerin in citrate buffer (citric acid and sodium citrate).

		Percent
20	Clindamycin phosphate	1.188
	Hydrous benzoyl peroxide	7.332
	Sodium metabisulfite	0.100
	Propyl gallate, 20% solution	0.500
	Disodiumedetate	0.050
	Citric acid monohydrate	0.096
25	Sodium citrate dihydrate	0.264
	Docusate sodium	0.025
	Carbomer 940	0.900
	Sodium hydroxide	0.140
	Glycerin	5.000
30	Purified water	84.405

EXAMPLE 5

35 Three-month stability data have been collected on Formulations 7, 8 and 9 at refrigeration (5° C) and room (23° C) temperatures:

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## PERCENT CLINDAMYCIN REMAINING

Temperature: 5° C

Formulation	7	8	9
1 month	99.4	98.1	96.3
2 months	98.5	98.8	97.7
3 months	98.6	96.7	94.1
6 months	97.3	98.0	96.2

5

Temperature: 23° C

Formulation	7	8	9
1 month	98.2	95.7	95.3
2 months	96.4	94.1	96.5
3 months	95.2	89.0	93.0
6 months	92.6		

## PERCENT BENZOYL PEROXIDE REMAINING

10

Temperature: 5° C

Formulation	7	8	9
1 month	102.6	99.2	99.4
2 months	101.6	98.9	99.2
3 months	100.6	97.9	93.8

Temperature: 23° C

15

Formulation	7	8	9
1 month	100.4	97.9	95.6
2 months	100.8	94.8	95.1
3 months	99.0	98.6	89.0

20

The compositions of further anti-acne gel formulations containing 1.19 percent clindamycin phosphate (equivalent to 1 percent clindamycin) and 5 percent benzoyl peroxide (on an anhydrous basis) are listed below:

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## PERCENT CLINDAMYCIN REMAINING

Temperature: 5° C

Formulation	7	8	9
1 month	99.4	98.1	96.3
2 months	98.5	98.8	97.7
3 months	98.6	96.7	94.1
6 months	97.3	98.0	96.2

5

Temperature: 23° C

Formulation	7	8	9
1 month	98.2	95.7	95.3
2 months	96.4	94.1	96.5
3 months	95.2	89.0	93.0
6 months	92.6		

## PERCENT BENZOYL PEROXIDE REMAINING

10

Temperature: 5° C

Formulation	7	8	9
1 month	102.6	99.2	99.4
2 months	101.6	98.9	99.2
3 months	100.6	97.9	93.8

Temperature: 23° C

15

Formulation	7	8	9
1 month	100.4	97.9	95.6
2 months	100.8	94.8	95.1
3 months	99.0	98.6	89.0

20

The compositions of further anti-acne gel formulations containing 1.19 percent clindamycin phosphate (equivalent to 1 percent clindamycin) and 5 percent benzoyl peroxide (on an anhydrous basis) are listed below:

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Formulation 10

Preparation containing microcrystalline cellulose, NF (Avicel RC-591) and colloidal magnesium aluminum silicate (Veegum HV) as gelling agents.

		Percent
	Clindamycin phosphate	1.190
	Benzoyl peroxide	5.000
5	Microcrystalline cellulose, NF	2.000
	Colloidal magnesium aluminum silicate	2.500
10	Disodiumedetate	0.050
	Docusate sodium	0.050
	Sodium citrate	0.200
	Purified water	89.010
15		

Formulation 11

Preparation containing microcrystalline cellulose (Avicel RC-591) and methylcellulose (Methocel A4M) as gelling agents.

		Percent
	Clindamycin phosphate	1.190
	Benzoyl peroxide	5.000
20	Microcrystalline cellulose (Avicel RC-591)	2.500
	Methylcellulose	0.500
25	Disodiumedetate	0.050
	Sodium dodecyulbenzenesulfonate	0.050
	Sodium citrate	0.200
	Purified water	93.210

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Formulation 12

Preparation containing hydroxypropylmethylcellulose (Methocel E4M) and xanthan gum (Keltrol T) as gelling agents.

	Percent
5	
Clindamycin phosphate	1.190
Benzoyl peroxide	5.000
Hydroxypropylmethylcellulose	1.500
Xanthan gum	0.500
10	
Disodiumedetate	0.050
Docusate sodium	0.050
Sodium citrate	0.200
Purified water	91.510

Formulation 13

Preparation containing colloidal magnesium aluminum silicate (Veegum HV) and hydroxypropylmethylcellulose (Methocel E4M) as gelling agents.

	Percent
20	
Clindamycin phosphate	1.190
Benzoyl peroxide	5.000
Colloidal magnesium aluminum silicate	2.000
Hydroxypropylmethylcellulose	1.500
25	
Disodiumedetate	0.050
Docusate sodium	0.050
Sodium citrate	0.200
Purified water	90.010

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Formulation 14

Preparation containing colloidal magnesium aluminum silicate (Veegum HV) and xanthan gum (Keltrol T) as gelling agents.

	Percent
5	
	Clindamycin phosphate
	1.190
	Benzoyl peroxide
	5.000
	Colloidal magnesium aluminum silicate
	2.000
	Xanthan gum
10	0.500
	Disodiumedetate
	0.050
	Docusate sodium
	0.050
	Sodium citrate
	0.200
	Purified water
	91.010

15 EXAMPLE 6

A 20 year old male applies 0.5 gms of Formulation to his face 4 times daily. After 10 days, the number of comedones begin to diminish. By the end of four weeks, the number of comedones declines significantly.

20 While particular embodiments of the invention have been described, it will be understood, of course, that the invention is not limited thereto since many obvious modifications can be made; and it is intended to include within this invention any such modifications as will fall within the scope of the appended claims. For example, it will be appreciated by those skilled in the art that various pharmaceutically acceptable derivatives, salts and prodrugs of clindamycin may be used in place of clindamycin and clindamycin phosphate. For example, clindamycin hydrochloride, clindamycin palmitate hydrochloride may be substituted for clindamycin. Also, various forms of peroxides may be used in place of hydrous benzoyl peroxide; i.e., diaryl peroxide, alkyl aryl peroxide, cycloalkyl aryl peroxide may be substituted for hydrous benzoyl peroxide. For example, lauroyl benzoyl peroxide, cyclohexyl carbanolyl benzoyl peroxide. Various sulfonate radical-containing surfactants may be used in place of dioctylsodium sulfosuccinate and sodium dodecylbenzene sulfonate. For example, diammonium lauryl sulfosuccinate, disodium laureth sulfosuccinate, sodium

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alpha olefin sulfonate, sodium dodecyl diphenyl ether disulfonate. Polyacrylic acid, commercially available under the trade name of Carbopols®, may be replaced by various other gelling agents, such as methylcellulose microcrystalline cellulose, hydroxypropyl methyl cellulose, colloidal magnesium aluminum silicate.

## CLAIMS:

1. A method of treating acne vulgaris in human patients comprising topically administering to said patients a composition comprising a therapeutically effective amount of benzoyl peroxide and clindamycin.  
5
2. The method of claim 1 wherein said benzoyl peroxide and clindamycin are dispersed in a pharmaceutically acceptable carrier.  
10
3. The method of claim 2 wherein said composition is a cream or a gel.  
15
4. The method of claim 3 wherein said composition comprises from about 0.25 to 2 percent, by weight, clindamycin.  
20
5. The method of claim 4, wherein said composition comprises from about 1 to 30 percent, by weight, benzoyl peroxide.  
25
6. The method of claim 5 wherein said composition comprises a surfactant comprising a sulfonic radical.  
30
7. The method of claim 6 wherein said surfactant is selected from the group consisting of dioctylsodium sulfosuccinate and sodium dodecylbenzene sulfonate.  
35
8. The method of claim 7 wherein said surfactant comprises from about 0.01 to about 1 percent, by weight, of said composition.  
9. The method of claim 8 wherein said composition further comprises a polyacrylic acid polymer.  
10. The method of claim 9, wherein said composition comprises about 1 percent, by weight, clindamycin, 5 percent, by

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weight, benzoyl peroxide, from about 0.1 to 0.2 percent, by weight, of a surfactant comprising a sulfonic acid radical and about 0.1 to about 0.2 percent, by weight, of a polyacrylic acid.

5 11. A topical composition for treating acne vulgaris in human patients comprising a therapeutically effective amount of benzoyl peroxide and clindamycin.

10 12. The composition of claim 11 wherein said benzoyl peroxide and clindamycin are dispersed in a pharmaceutically acceptable carrier.

15 13. The composition of claim 12 wherein said composition is a cream or gel.

14. The composition of claim 13 wherein said composition comprises from about 0.25 to 2 percent, by weight, clindamycin.

20 15. The composition of claim 14 wherein said composition comprises from about 2.5 to 20 percent, by weight, benzoyl peroxide.

16. The composition of claim 15 wherein said composition comprises a surfactant comprising a sulfonic radical.

25 17. The composition of claim 16 wherein said surfactant is selected from the group consisting of dioctylsodium sulfosuccinate that sodium dodecylbenzene sulfonate.

30 18. The composition of claim 17 wherein said surfactant comprises from about .001 to about 1 percent, by weight, of said composition.

19. The composition of claim 18 wherein said composition further comprises a polyacrylic acid polymer.

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20. The composition of claim 19, wherein said composition comprises about 1 percent, by weight, clindamycin, 5 percent, by weight, benzoyl peroxide, from about 0.1 to 0.2 percent, by weight, of surfactant comprising a sulfonic and radical about 0.01 to about 0.2 percent, by weight, of a polyacrylic acid.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 93/03325

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)<sup>6</sup>According to International Patent Classification (IPC) or to both National Classification and IPC  
Int.C1. 5 A61K7/48; A61K31/71

## II. FIELDS SEARCHED

Minimum Documentation Searched<sup>7</sup>

Classification System	Classification Symbols
Int.C1. 5	A61K

Documentation Searched other than Minimum Documentation  
to the Extent that such Documents are Included in the Fields Searched<sup>8</sup>III. DOCUMENTS CONSIDERED TO BE RELEVANT<sup>9</sup>

Category <sup>10</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
X	GB,A,2 150 436 (L'OREAL) 3 July 1985 cited in the application & US-A-4671956 see page 5; example 8 cited in the application ---	1-5, 9, 11-15, 19
Y	GB,A,2 090 135 (RORER INTERNATIONAL) 7 July 1982 cited in the application & US-A-4692329 see page 6; examples 5,9 ---	6-8, 10, 16-18, 20
Y	US,A,4 387 107 (KLEIN R.W. ET AL) 7 June 1983 cited in the application see column 5; example 4 ---	10, 20
Y		6-8, 16-18 -/-

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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## IV. CERTIFICATION

Date of the Actual Completion of the International Search

02 JULY 1993

Date of Mailing of this International Search Report

22.07.93

International Searching Authority

EUROPEAN PATENT OFFICE

Signature of Authorized Officer

BOULOIS D.

## III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

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A	US,A,3 969 516 (STOUGHTON R.B.) 13 July 1976 cited in the application -----	1-20

ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO.

US 9303325  
SA 73022

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